

In the Specification

Applicant presents replacement paragraphs below indicating the changes with insertions indicated by underlining and deletions indicated by strikeouts and/or double bracketing.

Please replace paragraph 2 beginning at page 16, line 13 with the amended paragraph/line as follows:

As described in ~~co-pending patent application US~~ U.S. Patent No. 6,239,116 ~~Serial No. 08/960,774~~, oligonucleotides containing an unmethylated CpG motif (i.e. TCCATGACGTTCTGACGTT; SEQ IN NO: 93), but not a control oligonucleotide (TCCATGAGCTTCCTGAGTCT; SEQ ID NO: 103) prevented the development of an inflammatory cellular infiltrate and eosinophilia in a murine model of asthma. Furthermore, the suppression of eosinophilic inflammation was associated with a suppression of Th2 response and induction of a Th1 response.

Please replace abridging paragraph beginning at page 32, line 32 with the amended paragraph/line as follows:

Preferred stabilized oligonucleotides of the instant invention have a modified backbone. It has been demonstrated that modification of the oligonucleotide backbone provides enhanced activity of the CpG oligonucleotides when administered *in vivo*. CpG constructs, including at least two phosphorothioate linkages at the 5' end of the oligonucleotide in multiple phosphorothioate linkages at the 3' end, preferably 5, provides maximal activity and protected the oligonucleotide from degradation by intracellular exo- and endo-nucleases. Other modified oligonucleotides include phosphodiester modified oligonucleotide, combinations of phosphodiester and phosphorothioate oligonucleotide, methylphosphonate, methylphosphorothioate, phosphorodithioate, and combinations thereof. Each of these combinations and their particular effects on immune cells is discussed in more detail in copending PCT Published Patent Applications claiming priority to U.S. Serial Nos. 08/738,652 (now issued as U.S. Patent No. 6,207,646) and 08/960,774 (now issued as U.S. Patent No. 6,239,116), filed on October 30, 1996 and October 30, 1997, respectively, the entire contents of which is hereby incorporated by reference. It is believed that these modified oligonucleotides

may show more stimulatory activity due to enhanced nuclease resistance, increased cellular uptake, increased protein binding, and/or altered intracellular localization.

Please replace abridging paragraph beginning at page 33, line 26 with the amended paragraph/line as follows:

The nucleic acid sequences of the invention which are useful for inducing immune remodeling are those broadly described above and ~~disclosed~~ disclosed in PCT Published Patent Applications claiming priority to U.S. Serial Nos. 08/738,652 (now issued as U.S. Patent No. 6,207,646) and 08/960,774 (now issued as U.S. Patent No. 6,239,116), filed on October 30, 1996 and October 30, 1997, respectively. Exemplary sequences include but are not limited to those immunostimulatory sequences shown in Table 1 as well as TCCATGTCGCTCCTGATGCT (SEQ ID NO: 47), TCCATGTCGTTCTGATGCT (SEQ ID NO: 48), TCGTCGTTTTGTCGTTTTGTCGTT (SEQ ID NO: 53), TCGTCGTTGTCGTTGTCGTT (SEQ ID NO: 89); TCGTCGTTTTGTCGTTTTGTCGTT (SEQ ID NO: 90), TCGTCGTTGTCGTTTTGTCGTT (SEQ ID NO: 91), GCGTGCGTTGTCGTTGTCGTT (SEQ ID NO: 92), TGTCGTTTGTGCGTTTGTGCGTT (SEQ ID NO: 94), TGTCGTTGTCGTTGTCGTT (SEQ ID NO: 96) TCGTCGTCGTCGTT (SEQ ID NO:97), TCCTGTCGTTCTTGTGCGTT (SEQ ID NO: 79), TCCTGTCGTTTTTTGTGCGTT (SEQ ID NO:81), TCGTCGCTGTCTGCCCTTCTT (SEQ ID NO:82), TCGTCGCTGTTGTCGTTTCTT (SEQ ID NO:83), TCGTCGTTTTGTGCGTTTTGTGCGTT (SEQ ID NO:90), TCGTCGTTGTCGTTTTGTGCGTT (SEQ ID NO:91) TGTCGTTGTCGTTGTCGTT (SEQ ID NO:96), TCCATGACGTTCTGACGTT (SEQ ID NO:100), GTCG(T/C)T (SEQ ID NO:101) and TGTCG(T/C)T (SEQ ID NO:102).

Please replace paragraph 2 beginning at page 34, line 12 with the amended paragraph/line as follows:

The stimulation index of a particular immunostimulatory CpG DNA can be tested in various immune cell assays. Preferably, the stimulation index of the immunostimulatory CpG DNA with regard to B cell proliferation is at least about 5, preferably at least about 10, more preferably at least about 15 and most preferably at least about 20 as determined by incorporation

of ^3H uridine in a murine B cell culture, which has been contacted with 20 μM of oligonucleotide for 20h at 37°C and has been pulsed with 1 μCi of ^3H uridine; and harvested and counted 4h later as described in detail in copending PCT Patent Application U.S. Serial No. 08/960,774 (now issued as U.S. Patent No. 6,239,116). For use *in vivo*, for example, to treat an immune system deficiency by stimulating a cell-mediated (local) immune response in a subject, it is important that the immunostimulatory CpG DNA be capable of effectively inducing cytokine secretion by APCs such as dendritic cells.

Please replace abridging paragraph beginning at page 34, line 32 with the amended paragraph/line as follows:

Preferably, the stimulation index of the CpG oligonucleotide with regard to B cell proliferation is at least about 5, preferably at least about 10, more preferably at least about 15 and most preferably at least about 20 as determined by incorporation of ^3H uridine in a murine B cell culture, which has been contacted with 20 μM of oligonucleotide for 20h at 37°C and has been pulsed with 1 μCi of ^3H uridine; and harvested and counted 4h later as described in detail in copending PCT Published Patent Applications claiming priority to U.S. Serial Nos. 08/738,652 (now issued as U.S. Patent No. 6,207,646) and 08/960,774 (now issued as U.S. Patent No. 6,239,116), filed on October 30, 1996 and October 30, 1997, respectively. For use *in vivo*, for example, it is important that the CpG oligonucleotide and cytokine be capable of effectively inducing activation of APC's such as dendritic cells. Oligonucleotides which can accomplish this are, for example, those oligonucleotides described in PCT Published Patent Applications claiming priority to U.S. Serial Nos. 08/738,652 (now issued as U.S. Patent No. 6,207,646) and 08/960,774 (now issued as U.S. Patent No. 6,239,116), filed on October 30, 1996 and October 30, 1997, respectively.